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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,645	07/12/2001	Yuri Kolesnikov	830010-2006.	3048

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EXAMINER	
WELLS, LAUREN Q	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,645	KOLESNIKOV ET AL.	
	Examiner	Art Unit	
	Lauren Q Wells	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *4,13 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-12 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8, 9, 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-17 are pending. Claims 4, 13, and 17 are withdrawn from consideration, as they are directed to non-elected subject matter. The Amendment filed 10/31/02, cancelled claim 18 and amended claim 17.

Election/Restrictions

Applicant's election with traverse of Restriction Requirement in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the species are each related to one another and directed to the same inventive concept, and examination of the generic claims does not impose a serious burden on the Examiner. This argument is not persuasive. The Examiner respectfully points out that number of possible combination of constituents in the instant invention is incredible. Thus, searching every combination would be impossible and therefore place a serious burden on the Examiner. Furthermore, the species are not all related. For example, a search of morphine does not necessitate finding lofentanil or buprenorphine, just as a search of ketamine does not necessitate finding MK801 or pyroloquinoline quinone.

The requirement is still deemed proper and is therefore made FINAL.

Note: While Applicant has amended claim 17, claim 17 is still withdrawn from consideration, as it is drawn to a method distinct from that of Group I. The Examiner respectfully points out that the combination of an NMDA receptor antagonist and an opiod analgesic is not a SPECIAL technical feature, as this feature is know, making it a technical feature (see US Patent No. 5,635,204). Thus, restriction between Group I and Group II, in light of the 10/31/02, amendment to claim 17, is proper and maintained.

Claim Rejections - 35 USC § 112

Claims 9-12 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a tolerance-attenuating dose of an NMDA receptor antagonist, does not reasonably provide enablement for a preventing dose of an NMDA receptor antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

The disclosure of the present invention is directed to a method of providing peripheral analgesia to a mammal comprising topical administration of a tolerance-attenuating or preventing dose of an NMDA receptor antagonist and an analgesic that functions through an opiate receptor. A skilled practitioner in the art using the teachings of Trujillo et al. (Brain Research) would be motivated to administer a composition comprising an NMDA receptor antagonist to reduce or eliminate opiod analgesic tolerance. However, preventing opiod analgesic tolerance is inconsistent with what is known in the art since (1) reduction of tolerance indicates that tolerance is decreased, but not prevented; and (2) elimination of tolerance indicates

that symptoms of tolerance may occur. Furthermore, prevention of opiod analgesic tolerance indicates that the subject *never* experiences any characteristics associated with opiod analgesic tolerance. Hence, the amount of guidance present in the specification, the absence of data indicating that the tolerance to opiod analgesics do not occur when NMDA receptor antagonists compositions are administered, and the state of the prior art indicating that the treatment using NMDA receptor antagonists in composition is possible, all indicate that treatment, not prevention of opiod analgesic tolerance is possible.

The amount of guidance necessary to perform Applicant's invention would result in undue experimentation because the skilled artisan would be forced to randomly test numerous conditions and amounts of NMDA receptor antagonists in composition to determine what NMDA receptor antagonists composition prevents opiod analgesic tolerance. Hence, the amount of guidance present in the specification fails to present the necessary instruction such that one can readily determine the appropriate composition of claims 9-12 and 14.

Note: The Examiner reviewed Applicant's specification, but noted that the data does not indicate prevention of opiod analgesic tolerance.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-8, 11-12 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) The term "derivative" in claims 1 and 11 is vague and indefinite, as it is not clear what compounds are encompassed by this term. The specification does not define this term and one of ordinary skill in the art would not be apprised of its meaning.

(ii) Claims 6 and 10 contain the trademark/trade name MK801. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an NMDA receptor antagonist and, accordingly, the identification/description is indefinite.

(ii) Claim 14 is vague and indefinite, as it is not clear what percent weight is being claimed. Is it the percent weight of the composition as a whole? What is it?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6, 9-12, 15 rejected under 35 U.S.C. 102(b) as being anticipated by Gevirtz et al. (5,635,204).

Gevirtz et al. teach a method for transdermal induction of anesthesia, analgesia or sedation by simultaneously, transdermally administering fentanyl, an alpha adrenergic agonist, and ketamine. Disclosed is a method of inducing anesthesia comprising transdermally

administering via a transdermal patch to the skin an amnesia producing drug selected from scopolamine, ketamine, and benzodiazepines, and after an amnesic state is produced, transdermally administering amounts of clonidine and fentanyl. Exemplified in the patches are carriers. Thus, the instant invention and Gevirtz et al. both teach a composition comprising an NMDA receptor antagonist (ketamine), an analgesic (fentanyl), and an excipient/carrier (polyisobutylene), and a method of applying the composition to the skin. See Example 1; Col. 5, line 35-Col. 6, line 50.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5 and 14 rejected under 35 U.S.C. 103(a) as being unpatentable over Gevirtz et al. as applied to claims 1-3, 6, 9-12, 15 above, and further in view of Nelson et al. (5,840,731) and Needham et al. (6,261,582).

Gevirtz et al. is applied as discussed above. The reference lacks morphine.

Nelson et al. teach a method and apparatus for administering analgesics. Fentanyl and morphine are disclosed as interchangeable analgesics that act on opiod pain receptors. See Col. 4, lines 11-42.

Needham et al. teach surgical methods and compositions thereof. Fentanyl and morphine are disclosed as interchangeable and combinable analgesics. See Col. 2, lines 60-64; Col. 15, lines 24-26.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the fentanyl of Gevirtz et al. for morphine because a) Gevirtz et al., Nelson et al, and Needham et al. are all directed to analgesic compositions; b) Nelson et al. and Needham et al. teach morphine and fentanyl as interchangeable opiod pain receptor analgesics; thus, one of ordinary skill in the art would be motivated to substitute morphine for fentanyl in the compositions of Gevirtz et al. because of the expectation of producing similar analgesic effects via the opiod pain receptor.

Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gevirtz et al. as applied to claims 1-3, 6, 9-12, 15 above, and further in view of Kaneko et al (Anesthesiology '94).

Kaneko et al. teach the synergistic antinociceptive interaction after epidural coadministration of morphine and lidocaine. See background.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the lidocaine of Kaneko et al. to the composition of the combined references because the combined references teach compositions comprising morphine, and Kaneko et al. teach that the coadministration of morphine and lidocaine produces synergistic analgesia.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gevirtz et al. in view of Smith et al. (6,194,000).

Gevirtz et al. teach a method for transdermal induction of anesthesia, analgesia or sedation. Disclosed is a method of inducing anesthesia comprising transdermally administering via a transdermal patch an amnesia producing drug selected from scopolamine, ketamine, and benzodiazepines, and after an amnesic state is produced, transdermally administering amounts of

clonidine and fentanyl. Exemplified in the patches are carriers. Thus, the instant invention and Gevirtz et al. both teach a composition comprising an NMDA receptor antagonist (ketamine), an analgesic (fentanyl), and an excipient/carrier (polyisobutylene), and a method of applying the composition to the skin. The reference lacks kits. See Example 1; Col. 5, line 35-Col. 6, line 50.

Smith et al. teach analgesic compositions comprising NMDA receptor antagonist. Disclosed are kits which comprise a plurality of unit dosage forms, in a container, the container including indicia indicative of a dosage regime. See abstract; Col. 9.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the transdermal patches of Gevirtz et al. in the kits of Smith et al. because a) Gevirtz et al. and Smith et al. are both directed to analgesic compositions comprising NMDA receptor antagonists, such as ketamine, and Smith et al. teach that kits cam comprise a plurality of unit dosage forms indicative of a dosage regime; thus, one of skill in the art would be motivated to teach the patches of Gevirtz et al. in kits because of the expectation of achieving a product that is specialized in different dose amount for different dosage regimes.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-5:30), with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Russell S. Travers can be reached on (703)308-4603. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular

communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw
November 22, 2002

SREENI PADMANABHAN
PRIMARY EXAMINER

12/8/02